Environmental health risk assessment : evaluation of some default assumptions

Chapter 10

Summary and General Discussion

In this thesis, the health risks of different environmental hazards such as heavy metals, PCBs/dioxin and indoor radon have been evaluated in several case studies. The process of risk assessment is a formal tool that can be applied to assess the potential adverse health effects in relation to environmental hazards. It is embedded in "Premises of Risk Management" of the Dutch National Environmental Policy Plan in 1989 (1). The process has been established in 1983 in general terms by the U.S. National Academy of Science/National Research Council. This committee defines risk assessment as 'estimating the magnitude, likelihood and uncertainties of environmentally induced health effects'. The process generally exists of four steps: hazard identification, exposure assessment, dose-response assessment and risk characterization (2).

The results of a risk assessment together with social, economic and political aspects are integrated into the risk management process, to formulate decisions aimed to protect public health.

As part of the risk characterization step, the uncertainties in the successive steps of the assessment process have to be described. These uncertainties are most commonly directed to the limited scientific knowledge to interpret the available data and furthermore, to the lack of available data (3-6). In order to deal with uncertainty in health risk assessments default assumptions have to be applied. Default assumptions are generic assumptions based on general knowledge, to fill in data gaps, and are furthermore used as a policy option for dealing with disagreements in models and theories (7). The use of default assumptions in risk assessment is matter of debate (4,6-10). Some authors comment that these assumptions are conservative and that it is not always clear on what judgements they are based; others argue that default assumptions enhance the uniformity of risk assessments. The National Academy of Science and the National Research Council stated in their follow-up report in 1994 (11) that the merits and effects of risk assessments will be enhanced by generating more data and by relying on fewer default assumptions, although default assumptions are justified as screening tools. In order to be able to rely on fewer default assumptions, the research underlying the risk assessment process has to be improved and results have to be effectively incorporated into the risk assessment process (3,6,12-15). Risk assessment, research and risk management are interrelated, and a feedback loop is postulated between risk management, risk assessment and research (3,11).

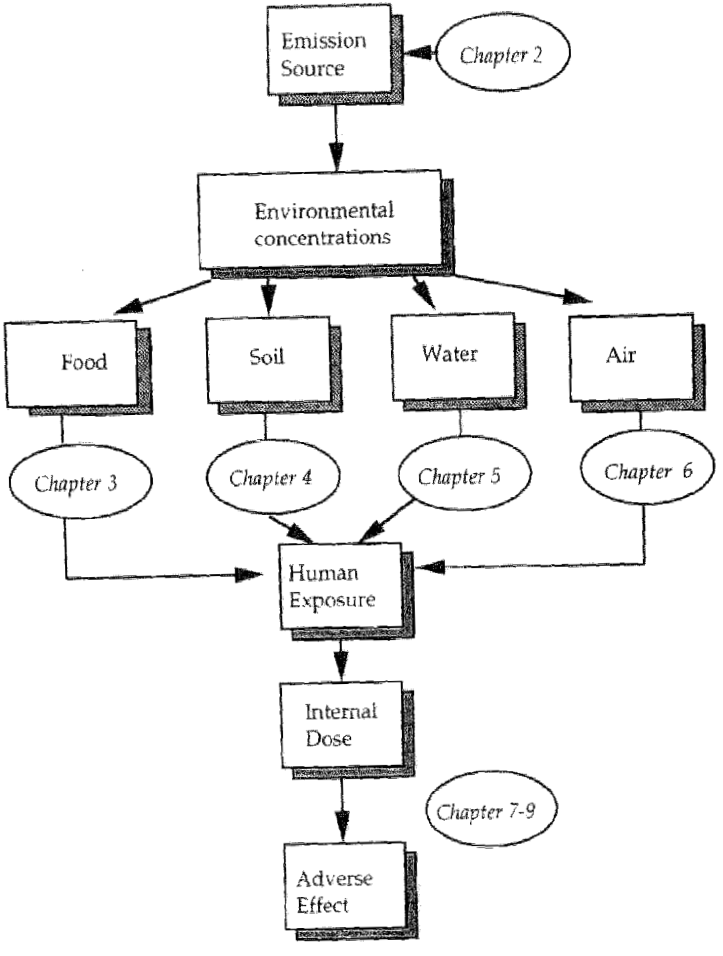
In addition to the risk assessment process, the environmental health chain can be used to evaluate the potential health risks of environmental hazards. The environmental health chain is characterized by a continuum of events: from the emission from a source into the environment to the final adverse health effects (3).

The chapters in this thesis have been structured along the environmental health chain as illustrated in Figure 10.1. Exposure assessment as part One of this thesis, concentrates on the first part of the chain: from emission from a source into the environment to environmental concentration to human exposure to internal dose, while dose-response assessment (part Two) concentrates on the last part of the chain: from human exposure to internal dose and to the ultimate adverse health effects (3).

In general, there are three different approaches to estimate exposure to an environmental agent: the direct, the reconstructive and the predictive approach (10,16,17). The predictive approach has been used in part One of this thesis by applying different scenario models. This method is predominantly used in environmental health studies (17-23) and has been developed as a default method, to be used if measurements are unavailable (6). Additionally, to the use of scenario models, location-specific measurements have been performed to replace some default assumptions and to provide more realistic estimates of exposure. Subsequently, the estimated exposure added to background exposure levels, has been compared to existing health-based standards (e.g. TDI) to determine whether there is any potential health impact. The first two case studies in this thesis address PCB and dioxin exposure.

Chapter 2 describes a human health risk assessment in relation to dioxin/PCB emission concerning three newly proposed waste incinerators in The Netherlands. The incineration of solid waste is regarded to represent the main source of dioxin exposure for the general population (24,25). Before a waste incinerator can be installed it is generally required that a health risk assessment is performed as part of the environmental impact assessment (EIA) procedure. The only way to estimate exposure that might arise from future actions, is by using the predictive approach (5). The current exposure model has been designed by using worst-case assumptions to estimate additional exposure to the PCB/dioxin emission (expressed as toxic equivalents) at the maximally exposed location as estimated in the EIAs. From the risk management point of view, it is acceptable to use a worst-case scenario in order to protect public health.

Although numerous uncertainties are inherent to this exposure model, the major uncertainty in this risk assessment appears to be the PCB-TEQ emission from a WI. In monitoring the emission from WIs, only the dioxins (expressed as TEQ) have been taken in consideration (26). Newly to be constructed WIs



Case 1: Dioxin/PCBs

Chapter 2 → *PCB/Dioxin emission from a WI*
- *exposure scenario model*

Chapter 3 → *sediment pollution by PCBs*
- *site-specific measurements; eel*

Case 2: river Meuse

Chapter 4 → *River bank pollution by heavy metals*
- *exposure scenario model*
- *site-specific measurements; soils; vegetables*

Chapter 5 → *sediment pollution in freshwater lakes*
- *exposure scenario model*
- *site-specific measurements; sediment; surface water; suspended matter*

Case 3: Indoor radon

Chapter 6 → *soil/indoor measurements short/long term radon measurements*

Chapter 7
Chapter 8 → *Genetic biomarkers linearity dose-reponse relationship*
Chapter 9

Figure 10.1: The case studies and chapters structured along the environmental health chain

have to meet with emission standards by the Waste Incinerator Act from 1993. The dioxin-TEQ emission standard has been set on 0.1 ng TEQ/m^3. However, the emission of PCBs by a WI is not regulated. Quantitative information about the PCBs and in particular the PCB-TEQ emission is not available. The emission of PCBs as estimated in the EIAs is based on the amount of PCBs in the waste taken different extraction efficiencies into consideration. In calculating the health risk for the different PCB-TEQ emission scenarios, we have assumed that the contribution of the coplanar PCBs to the total PCB emission is a fixed percentage (10%). The calculated total (additional and background) exposure to dioxin-TEQ and PCB-TEQ has been compared to the health based standard (TDI) of 10 pg TEQ/kg bw per day as recommended by the WHO. For a few PCB-TEQ emission scenarios the TDI will be exceeded. However, a study performed in The Netherlands recently, indicated that the PCB-TEQ emission accounted for only a few percents of the total dioxin-TEQ emission (26). This suggests that the calculated PCB-TEQ emission in our study overpredicts reality and as a consequence also the to be expected exposure risks are overestimated. From this study, it is concluded that the major uncertainty in exposure risk assessment for a population surrounding a WI, refers to PCB emission. To regulate the PCB-TEQ emission by a WI, it is recommended that the dioxin-TEQ emission standard of 0.1 ng TEQ/m^3 matches the TEQ emission of both dioxins and PCBs.

The second case study with respect to PCB and dioxin exposure describes the health risks in relation to consumption of contaminated fish (*chapter 3*). The sediments of brooks in the south-west part in The Netherlands are polluted by various heavy metals, insecticides and PCBs. Public health officials were concerned about the hazards associated with the consumption of contaminated fish caught at these brooks by recreational anglers. Recreational anglers fishing in these brooks, tended to consume more fish and consequently fish contaminants, than the general population and therefore appeared to be at higher exposure risk. Location-specific measurements of PCBs, insecticides and mercury in three eelsamples (each consisting of 25 specimen) were performed. The contaminant concentrations in the eel samples appeared to be low in comparison to eel samples from Dutch rivers. Only for the PCBs (as toxic equivalents) the potential human health risk associated with consumption of contaminated eel has been evaluated. Recreational anglers in this area appear to consume 10 eels per week on average during the months May till October. This study demonstrates the huge impact of data on fish consumption rates on the final outcome of the exposure assessment. Considering background exposure to TEQ, the daily intake for anglers in this area appears to be 344 pg TEQ, which is below the current TDI of 10 pg TEQ/kg bw. Eel consumption by recreational anglers in this area therefore does not impose a possible health risk.

In *chapter 5* exposure to river sediment derived contaminants has been evaluated. The sediments of two freshwater lakes along the river Meuse are highly polluted by heavy metals and PAHs. The lakes have been created by excavation of minerals, and are nowadays used for recreational activities such as swimming, surfing and fishing. A standard exposure scenario model has been applied to estimate exposure with respect to these recreational activities. The concentrations of the contaminants in sediments are the source for the model, that furthermore predicts the environmental concentration at the point of human exposure. For instance, the model calculates the contaminant concentration in fish. By incorporating location-specific measurements of the contaminant concentration in surface water and suspended matter, the exposure assessments have been refined and the uncertainties reduced. A possible health risk as a consequence of exposure to Zn and Pb is indicated in relation to the recreational activities on both lakes. The consumption of contaminated fish is the dominant exposure pathway for the heavy metals (e.g. As, Cd, Cu, Pb and Zn) and PAHs (as B(a)P equivalents). Taken location-specific measurements into account, the risks of consumption of contaminated fish are reduced by more than two orders of magnitude implying that the health-based standards are not exceeded.

As previously described exposure through the ingestion of contaminated fish is also the only relevant exposure pathway in relation to sediment pollution of the two brooks located in the south-west part of The Netherlands (Chapter 3). Upon application of the same exposure scenario model, it is indicated that the location-specific levels of contaminants in eel, e.g. heavy metals, specifically Hg, are actually higher than calculated. The total mercury content which exists almost entirely of methylmercury, has been analyzed in the fillet of the fish (27). A comparison between predicted vs measured concentrations in fish is not possible for the other compounds (e.g. PCBs and insecticides) because of the lack of appropriate data of the sediments. This underestimation of eel mercury content by the exposure assessment model can be due to several causes. Accumulation of contaminants in fish can occur via different processes; by diffusion across the gill or through components of the foodchain (27,28). Physiochemical properties of the contaminant and the habitat and physiological properties of the organism comprise the most important factors (29). Accumulation of mercury in eel predominantly occurs by accumulation through the foodchain (30). The concentration in fish has been predicted by a general contaminant-specific bioconcentration factor, which expresses contaminant partitioning between fish and surface water. The BCF (mean value) represents the potential for accumulation of a compound (29). Several physical, chemical and biological parameters may contribute to the variation in BCF, such as fish species, age of the fish, dietary habits of the fish and chemical properties of the sediment (30,31). Moreover, the BCF for mercury is based on total mercury concentration in fish and surface water. The

speciation of mercury (inorganic, organic and methylmercury) is not taken into consideration (30). In addition, methylmercury can be formed from inorganic mercury in fish, which also contributes to the uncertainty of the general BCF (30). Concentrations in fish estimated by means of a general BCF value are therefore of limited accuracy (32).

This comparison between results from studies described in chapters 3 and 5, clearly demonstrates the impact of intercompartimental transfer data on the final results of the exposure assessment, e.g. in relation to indirect exposure.

Due to the uncertainty of the BCF it is recommended to use location-specific measurements of fish, specifically bottom feeding fish, to estimate the possible health risk in relation to the consumption of locally caught fish. In addition, information on local fish consumption rates and patterns is necessary to estimate the exposure correctly.

Next to the recreational function of the river, the banks of the river Meuse in The Netherlands and also in France and in a part of Belgium are commonly used for agriculture practice (e.g. pasture, arable farming and vegetable gardens). The frequent flooding of the river in these countries, however causes a more or less serious contamination of the soils in these areas. The agricultural function of the river is threatened by deposition of sludge and pollutants on the river banks. We have investigated the possible health risks in relation to the Dutch river bank pollution in the Borgharen-Itteren area after the flooding of the river during the winter of 1993-1994 (*chapter 4*). It was found that the river banks soils, and crops grown on these soils as well as cattle pasture may be burdened to a considerable degree by heavy metals.

After modeling the exposure scenario for agricultural situations, the highest intake appears associated with the consumption of meat and dairy products and results in a health risk for the general population in relation to Cd and Pb contamination of the river banks in the whole area under study. Incidentally, the health based standards for As and Zn are exceeded by children. However, it is assumed that 10% of the consumed meat and dairy products comes from the contaminated area, which is a conservative assumption and therefore, is not included in the realistic estimate of exposure based on location-specific measurements. These measurements were performed for quantification of the indirect exposure pathway (consumption of home grown vegetables) in view of the uncertainties regarding soil-plant transfer. The heavy metal concentrations in plants are modeled by contaminant-specific bioconcentration factors. In view of the large uncertainties on intercompartimental transfer parameters, as has been discussed previously, leafy vegetables (e.g. lettuce), legumes (e.g. beans) and root vegetables (e.g. potatoes) have been grown in 6 experimental gardens in the area. The heavy metal levels in the crops appear within normal background levels, except for one garden located in an area with

a flooding frequency of once every two years, where the cadmium concentration in lettuce and potatoes exceeded the maximum permissible concentration according to the Commodities Act. From this study it can be concluded that the measured mean contaminant-specific bioconcentration factor for the different plants appeared to be lower than the default value, except for Cu for which the measured mean values were higher. This implies that human exposure through the ingestion of vegetables has been overestimated by 70% for respectively Cd, Pb and Zn and underestimated by 27 % for Cu. This demonstrates as in chapter 3 and 5 the influence of the transfer data on the final results of the exposure assessment. On the basis of the realistic estimate of exposure for the general population, a possible health risk for children as well as for adults is only indicated in relation with lead and cadmium contaminations of the river banks of the Meuse which are frequently inundated (flooding frequency every two years). Children appear to be a sensitive subpopulation to irreversible brain damage and learning disabilities resulting from lead exposure because of which a health based standard has been formulated specifically for children (33).

In summary, the emission from a source is the first step in the environmental health chain from source to effect (Figure 10.1) and the uncertainty of the emission (*chapter 2*) at the beginning of the chain also influences the other steps through the chain and ultimately the assessment of the health risk related to the emission (6). To improve exposure assessment, location-specific measurements in the environmental compartments (*chapter 3-5*) have been performed. However, there are still uncertainties in the intervening steps from the environmental compartments to human exposure. Therefore, the estimated exposures in part One of this thesis should not be interpreted as the absolute measures of actual exposure. Direct measurements of exposure are the only way to determine actual exposure and to validate and verify the exposure model (6). However, it is very difficult for instance, to measure the additional exposure directly for the general population in relation to the emission of dioxin and PCBs by a WI, because the additional exposure is relatively low and is within background levels. Furthermore, a WI is not the only source which contributes to the exposure to dioxin and PCBs.

The estimated exposures to an environmental agent in part One of this thesis have been compared with established health based standards (e.g. TDI). The TDI refers to the reference dose of a substance that can be taken in without identifiable risk of lifetime exposure. In general, the TDI is derived from a no-effect level in animal studies divided by safety factors (e.g. for intra- and interspecies variation). This creates a safety margin for the most sensitive persons, examples are children, pregnant women and elderly people. Averaged exposure over a lifetime is calculated by taking the daily exposure of children (0-

6 years) and adults (7-70 years) into account.

The results of the health risk assessment in relation to the soil contamination after the flooding of the river Meuse indicate that incidentally the TDI for Zn and As is exceeded by children (*chapter 4*). Consequences for health of exceeding the TDI during childhood are difficult to interpret (34). However, average Zn and As exposures over lifetime are lower than the TDI, which indicates that a possible health risk in relation to these heavy metals is relatively low.

Realistic risk assessments do not only depend on a better characterization of exposure assessment but also on a better characterization of dose-response assessment. Obviously, comparisons of outcomes of exposure assessments with established TDI values can hardly fulfil this requirement. Part Two of this thesis deals with an attempt to study biological responses to low dose exposure, in particular in relation to indoor radon exposure, and concentrates on the last part of the source-to effect continuum from human exposure (*chapter 6*) to internal dose to adverse health effects (*chapter 7-9*).

Indoor radon exposure contributes largely (more than 50%) to the dose-equivalent received by the general population from all sources of radiation. The major health risk in relation to indoor radon exposure is thought to be lung cancer. The cancer risk for the general population is calculated on the basis of linear extrapolation from epidemiological data of underground miners exposed to high radon levels. The cancer risk estimation in relation to indoor radon exposure indicates that radon exposure may contribute up to 8% respectively 10% to the annual lung cancer risk among the general population in The Netherlands and Belgium. However, epidemiological studies on the relation between indoor radon exposure and lung cancer have shown conflicting results and the actual risk for the general population of exposure to low levels of indoor radon is still uncertain (35-39). In addition, it is suggested that indoor radon exposure causes extrapulmonary cancers (e.g. leukaemia, melanoma, kidney and prostate) which indicates that the carcinogenic effect may not be restricted to the lung epithelium (40-42). Although not actually measuring disease, genetic biomarkers provide an alternative to epidemiological studies, because of their potential to improve validity and reducing bias in analyzing relatively smaller size populations. Higher frequencies of chromosome aberrations and *hprt* mutations in peripheral lymphocytes have been found in populations living in areas with increased background radiation (43-44). For this reason multiple biomarkers, indicative for DNA damage, have been studied along an indoor radon concentration gradient, in populations living in the Dutch-Belgian border region (*chapter 7-9*).

To establish an exposure gradient from high to low levels of indoor radon, a survey of radon concentrations in soils and dwellings in this region has been

conducted (*chapter 6*). The geological structure of the subsoil in this region is characterized by large differences in uranium-rich to uranium-poor rocks and soils. Uranium and radium distributions in soils and rocks are the major sources of indoor radon. In addition, we have studied whether soil gas radon measurements are a suitable indicator to predict the radon potential of this region.

The first study on indoor radon air levels has been performed in February 1992 in 116 dwellings in the township of Visé (radon prone area) by means of a charcoal detector for 24h. The average radon concentration was 116 Bq m^{-3}. A significant relation has been observed between the indoor air concentrations and the geology of the subsoil. As expected, in the low background area, the indoor radon concentrations in dwellings (n=42) determined by the same method, are much lower. Furthermore, in the same region time-integrated alpha-track measurements (3 months) of indoor radon exposure show similar results. In addition, the indoor radon levels are lower at higher house floors. Soil gas radon levels surrounding 26 houses, correlate with indoor radon exposure. Soil gas measurements can be used to predict the radon potential of an area. However, the method is not useful to predict small differences in indoor air levels. By this survey of radon concentrations in dwellings, an exposure gradient from low to high indoor radon levels has been established which has been used in the multiple genetic biomarker studies.

Chapter 7 to 9 describe the cytogenetic biomarker studies in relation to indoor radon exposure in populations living in the Dutch-Belgian border region. A pilot study was conducted to test the feasibility of genetic biomarker analysis (e.g. micronuclei, chromosome aberrations, sister chromatid exchanges and *hprt* mutation frequency) in relation to indoor radon exposure (*chapter 7*). 11 non-smoking participants with different indoor radon levels were selected to participate in the study. During one day in the spring of 1991, concentrations of radon gas in the living room were determined by means of a charcoal canister. From this study, it was concluded that biomarker analysis in humans in relation with indoor exposure to radon is readily achievable. The follow-up study has been directed at cytogenetic analysis in a larger population and in a combination with more accurate measurements of indoor radon levels by time integrated alpha-track detectors over a 3 months period (*chapter 8 and 9*). 24 people participated in the follow-up study. The results of the feasibility study and the follow-up study did not demonstrate a relation between indoor radon exposure and the induction of micronuclei, chromosome aberrations and sister chromatid exchanges in peripheral blood of exposed subjects. In addition, in both studies the *hprt* mutation frequency (logarithmic transformed) in peripheral lymphocytes of the exposed subjects was significantly and negatively correlated to indoor radon exposure. Furthermore, the SCE-frequency significantly correlated with cigarette smoking behaviour in both studies and a

significant correlation with subject's age has been found for the *hprt* mutation frequency and for the occurrence of micronuclei (feasibility study) and SCE's (follow-up study).

As mentioned before, Bridges and co-workers found a significant dose-dependent increase in *hprt* mutation frequency in a population environmentally exposed to indoor radon. (44). However, in their follow-up study, which has been recently published, no significant positive or negative association between indoor radon exposure and *hprt* mutation frequency has been observed (45). This follow-up study exists of three different data sets, which also include the first study by Bridges et al (44). In total 66 occupants of 41 houses have been included into the study. The indoor radon concentration ranges from 18 to 484 Bq m^{-3}. However, in one data set (including 33 participants), a significant negative correlation between indoor radon levels and *hprt* mutation frequency has been found, which confirms our finding presented in chapter 7 and 9.

Also after combining our *hprt* mutation frequency data from the feasibility study and the follow-up study (in total 33 participants), a significant negative correlation between indoor radon levels and *hprt* mutations is observed ($R= 0.46$; $p < 0.01$).

Additionally, a study performed among former uranium miners from the Radium Hill uranium mine in south Australia showed no relation between the *hprt* mutation rates and previously occupational exposure to radon (46).

There seems to be no biological indication for extrapulmonary effects of radon exposure. It can be concluded from these results that no linear relationship has been observed between indoor radon exposure and genetic biomarkers, which are indicative for DNA damage as early markers for carcinogenesis. Obviously, the current theoretical models for radon cancer risk assessment of linear extrapolation to low dose do not consider these findings.

In general, epidemiological studies report conflicting results. A recently published epidemiological study, in which the data from 11 cohort studies of radon exposed underground miners have been pooled, confirms the linearity of low dose, suggesting that low-level radon exposure in dwellings indicates some risk (47). To date, epidemiological studies on indoor radon exposure of the general population do mostly not show a excess cancer risk (48). Interestingly, Cohen recently demonstrated a negative correlation between domestic radon exposure and lung cancer (49). Furthermore, although in vitro studies indicate that radon can cause cell transformation, changes in chromosome structures and gene mutations, DNA repair processes appear to be important at the low dose range, suggesting a non-linearity at low dose (49,50).

In conclusion, there remains considerable uncertainty in relation to the cancer risk of domestic radon exposure for the general population; our attempt to reduce uncertainties by studying genetic biomarkers instead of cancer incidence, was unsuccessful within this respect.

In this thesis, several case studies in relation to environmental health risk assessment have been described. The case studies intended to improve exposure or dose-response assessment by replacing some default assumptions. Part One of this thesis deals with exposure assessment. Exposure to the environmental agents has been determined by an exposure scenario model (default method) and by location-specific measurements. In general, the location-specific measurements provide a more realistic estimate of exposure than can be obtained with standard models. The default exposure scenario model can be used as a screening method to estimate exposure and identify important exposure pathways, which can be addressed by location-specific measurements. The NAS committee has recently proposed such an iterative approach of risk assessment (11). An iterative approach to risk assessment will start with relatively inexpensive screening techniques (e.g. exposure scenario models), which are mostly conservative. Refined risk assessments use more site-specific exposure information and reduce the extent to which default assumptions are required. However, the question whether to conduct more location-specific measurements in order to improve exposure assessment, has to be weighed against the value of the information obtained. For instance, in Chapter 5 it has been demonstrated that it is not necessary to perform location-specific measurements in relation to recreational activities, when exposure through ingestion of contaminated fish is not a relevant exposure pathway.

The aim of the case study described in part Two of this thesis, was to evaluate the linearity at low-dose of the dose-response curve of domestic radon exposure and cancer risks. No linear relationship has been observed between domestic radon levels and multiple genetic biomarkers indicative for DNA damage. In the general population conflicting epidemiological data on the cancer risk of radon with respect to indoor exposure have been reported. Furthermore, conflicting results are observed from *in vitro* studies, and also from genetic biomarker studies in the general population. As a default assumption, linearity of response in low radon exposure ranges may be criticized.

It seems that at low dose the uncertainty in dose-response assessment is larger than the uncertainty in exposure assessment which indicates the major challenge for the science of risk analysis in the future.

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Samenvatting

De mens wordt via diverse contactmedia (bodem, lucht, voedsel en water) blootgesteld aan verschillende agentia in het milieu. Voor het in kaart brengen van de gezondheidsrisico's gepaard gaande met blootstelling aan deze agentia, kan gebruik worden gemaakt van de "bron-tot-risico" ketenbenadering, en van een model van risicobeoordeling en risicobeheersing. Het eerste gangbare model is ontwikkeld door de National Academy of Science in de VS in 1983. Deze commissie omschrijft het begrip risicobeoordeling als een karakterisering van mogelijke schadelijke gezondheidseffecten in relatie tot blootstelling van de mens aan gevaarlijke milieufactoren. In het algemeen wordt dit proces nader onderverdeeld in 4 fasen: het identificeren van gevaren, het vaststellen van het blootstellingsniveau (aangeduid als "exposure assessment"), het vaststellen van een relatie tussen dosis en effect (aangeduid als "dose-response assessment"), en een karakterisering van het risico op basis van de eerste drie fasen in een vorm die geschikt is voor de risicobeheersing. Voor het beoordelen van risico's is wetenschappelijke kennis nodig, welke eveneens is opgenomen in het model. Het beslissen over de toelaatbaarheid van risico's en het treffen van maatregelen zijn onderdeel van de risicobeheersing.

Bij de laatste fase van de risicobeoordeling, de risicokarakterisering, worden de onzekerheden inherent aan voorgaande fasen van de beoordeling, in kaart gebracht. Deze onzekerheid is enerzijds het resultaat aan gebrek aan wetenschappelijke kennis en anderzijds het gevolg van gebrek aan gegevens. Bij gebrek aan gegevens en kennis wordt gebruik gemaakt van plausibele veronderstellingen ("default assumptions") om tot een beoordeling van het risico te komen. Voorbeeld van een plausibele veronderstelling is de lineaire dosis-respons relatie bij lage doses van genotoxische stoffen. Er is veel discussie gaande over het gebruik van plausibele veronderstellingen in de risicobeoordeling; met name de veronderstellingen die conservatief van aard zijn worden bekritiseerd. Men neemt aan dat het gebruik van deze conservatieve veronderstellingen eerder zal leiden tot een overschatting dan tot een onderschatting van het risico.

Het doel van dit proefschrift is om aan de hand van enkele voorbeeldstudies de gezondheidsrisico's van verschillende milieu-agentia te evalueren, waarbij de nadruk ligt op de evaluatie/vervanging van enkele plausibele veronderstellingen bij zowel de blootstellingsbeoordeling (Deel 1) als de dosis-responsbeoordeling (Deel 2).

In de inleiding wordt de "bron-tot-risico" ketenbenadering kort samengevat. Vervolgens wordt het proces van de risicobeoordeling en risicobeheersing beschreven, waarbij eveneens wordt ingegaan op de onzekerheid en het gebruik van plausibele veronderstellingen in de risicobeoordeling. Daarna

wordt kort beschreven hoe door middel van wetenschappelijk onderzoek het beoordelen van de blootstelling enerzijds en van de dosis-respons relatie anderzijds kan worden verbeterd. In dit proefschrift is voor de indeling van de hoofdstukken de ketenbenadering van bron naar risico gevolgd.

Zoals eerder vermeld beschrijft Deel 1 van dit proefschrift casuïstiek waarbij de gezondheidsrisico's worden geschat in een specifieke blootstellingssituatie. De blootstelling wordt enerzijds geschat aan de hand van een blootstellingsmodel en anderzijds wordt gebruik gemaakt van locatie-specifieke metingen in de verschillende milieucompartimenten. Een blootstellingsmodel of scenario kan worden beschouwd als een plausibele veronderstelling.

Het in de Hoofdstukken 2 en 3 beschreven onderzoek heeft betrekking op de schatting van de blootstelling ten aanzien van dioxinen en PCB's. Voor kwantificering van het gezondheidsrisico in relatie tot de emissie van dioxinen en dioxine-achtige PCB's door een nieuw te bouwen afvalverbrandingsinstallatie, is uitgegaan van een "worst-case" benadering waarbij voor de slechts denkbare situatie het gezondheidsrisico met behulp van een blootstellingsmodel is geschat (Hoofdstuk 2). Uit de resultaten blijkt dat het voorstelbaar is dat bij bepaalde emissiescenario's voor PCB's met een dioxine-achtige toxiciteit de momentane TDI van 10 pg TEQ/kg lichaamsgewicht wordt overschreden. Alhoewel in het blootstellingsmodel verschillende onzekerheden een rol spelen, bestaat de grootste onzekerheid in de aanname van de uitworp van PCB's door een afvalverbrandingsinstallatie. Om deze onzekerheid te beheersen wordt aanbevolen om de emissie- grenswaarde van 0.1 ng TEQ/m^3 zoals deze in het Besluit luchtemissies afvalverbranding 1993 is vastgesteld voor de uitworp van dioxinen en furanen, ook te betrekken op PCB's met een dioxine-activiteit.

De kwantificering van het gezondheidsrisico bij consumptie van verontreinigde aal uit twee beken in West-Brabant wordt beschreven in Hoofdstuk 3. De gemeten concentraties van PCB's, kwik en organochloor-pesticiden in 3 aalmonsters (per monster 25 alen) afkomstig uit deze wateren, zijn relatief laag en vergelijkbaar met aal uit schone binnenwateren. Sportvissers kunnen als een risicogroep worden beschouwd gelet op het feit dat de sportvissers veel en/of vaak zelf gevangen vis die verontreinigd kan zijn, consumeren. Sportvissers die vissen op deze wateren, blijken gedurende de maanden mei tot oktober gemiddeld 10 alen per week te consumeren. Op basis van gemeten gehalten van 3 mono-ortho PCB-congeneren in de bemonsterde aal wordt geen gezondheidsrisico verwacht bij de door de sportvissers opgegeven visconsumptie. De additionele blootstelling als gevolg van de consumptie van verontreinigde vis draagt voor meer dan 80% bij aan de uiteindelijke blootstelling.

De mogelijke gezondheidsrisico's in relatie tot een verontreiniging van de onderwaterbodem van twee Maasplassen in Limburg worden in kaart gebracht in Hoofdstuk 5. De onderwaterbodems zijn onder andere verontreinigd met zware metalen en PAK's. De Maasplassen worden frequent gebruikt voor recreatieve activiteiten zoals bijvoorbeeld zwemmen, vissen en surfen. Aan de hand van een gestandaardiseerd blootstellingsmodel is een schatting gemaakt van het blootstellingsrisico in relatie tot deze recreatieve activiteiten. De ingestie van verontreinigde vis blijkt eveneens de belangrijkste bijdrage te leveren aan de totale blootstelling ten aanzien van een verontreiniging van de onderwaterbodem met zware metalen en PAK. Toepassing van het model leidt tot de voorspelling dat de TDI voor Zn en Pb wordt overschreden. Naast het meten van het gehalte aan zware metalen en PAK's in de onderwaterbodem zijn eveneens locatie-specifieke metingen in het oppervlaktewater en het zwevend stof uitgevoerd, teneinde de blootstellingsschatting te verbeteren en de onzekerheden te reduceren. Op basis van de zware metalenconcentratie in de contactmedia blijkt de blootstelling tengevolge van de ingestie van verontreinigde vis marginaal in vergelijking met de resultaten verkregen op basis van het gestandaardiseerde model. Het gezondheidsrisico berekend aan de hand van de locatie-specifieke metingen, is verwaarloosbaar. Geconcludeerd kan worden dat overdrachtsfactoren van onderwaterbodem naar oppervlaktewater en het zwevend stof zoals gehanteerd in het gestandaardiseerde model, een grote invloed hebben op de uiteindelijke blootstellingsschatting.

De oevergronden van de Maas hebben voornamelijk een agrarische functie. Inundatie van de oevergronden van de Maas en de daarop verbouwde gewassen vindt variërend in omvang in verschillende periodes en seizoenen van het jaar plaats. In de winter van 1993-1994 zijn grote gedeeltes van de Maasoevers en aldaar voorkomende dorpen overstroomd. Bij overstromingen van de uiterwaarden en oevergronden wordt o.a. slib afgezet dat verhoogde gehalten aan zware metalen kan bevatten. De mogelijke gezondheidsrisico's na de overstroming van de Maas worden nader beschouwd in Hoofdstuk 4. Evenals in Hoofdstuk 5 zijn een gestandaardiseerd blootstellingsmodel en locatie-specifieke metingen gebruikt om de menselijke blootstelling in relatie tot de directe en indirecte blootstellingsroutes te kwantificeren. Toepassing van het model leidt voor het onderzoeksgebied Borgharen-Itteren tot de voorspelling dat de TDI voor Cd en Pb frequent wordt overschreden. De belangrijkste bijdrage aan de totale blootstelling wordt geleverd door de consumptie van ter plekke geproduceerde dierlijke voedingsmiddelen.

Kwantificering van transferprocessen van zware metalen van grond naar plant gaat gepaard met grote onzekerheden. Ter reductie van deze onzekerheidsfactor zijn in het onderzoeksgebied proeftuinen aangelegd, waarin aardappelen, stamslabonen en pluksla zijn uitgezet. Gebruik makend van het gestandaardiseerde model blijkt, dat de menselijke blootstelling via ingestie

van gewassen met 70% wordt overschat voor de metalen Cd, Pb en Zn en met 27% wordt onderschat voor het metaal Cu in vergelijking met resultaten verkregen op basis van de locatie-specifieke metingen. Ook uit dit onderzoek blijkt dat transferparameters in het model een grote invloed hebben op de uiteindelijke schatting van de blootstelling. Op basis van de gemeten zware metalengehalten in de contactmedia (bodem en gewasingestie) en rekening houdend met de achtergrondblootstelling, blijkt dat de TDI voor cadmium en de TDI voor lood door kinderen wordt overschreden in gebieden met een overstromingsfrequentie van 1 maal per 2 jaar.

In Deel 2 van dit proefschrift ligt de nadruk op de evaluatie van de lineariteit van de dosis-effect relatie tussen het kankerrisico enerzijds en blootstelling aan radon in het lage dosisgebied anderzijds. Zoals eerder vermeld is de lineariteit van de dosis-respons relatie in het lage dosisgebied van ioniserende straling een voorbeeld van een plausibele veronderstelling. De carcinogeniteit van radon en vervalprodukten is goed beschreven bij uranium mijnwerkers. Sterfte aan longtumoren wordt in het algemeen beschouwd als het belangrijkste effect van blootstelling aan radon. De lineaire dosis-effect relatie dient als basis voor de schatting van het longkankerrisico voor de algemene bevolking. Echter, de onzekerheid in de schatting van het kankerrisico van radon blootstelling in het lage blootstellingsgebied zoals voorkomend in woningen is groot. Resultaten uit epidemiologisch onderzoek naar de relatie tussen binnenhuisblootstelling aan radon en longkankersterfte zijn tegenstrijdig. Voorts zijn er aanwijzingen dat andere vormen van kanker dan longkanker, zoals melanomen, prostaat- en nierkanker, door radon kunnen worden veroorzaakt. In het veld van de moleculaire biologie zijn technieken voor het vaststellen van genetische schade ontwikkeld. Alhoewel met deze technieken geen ziekte wordt gedetecteerd, kunnen ze een alternatief vormen voor epidemiologisch onderzoek. In dit kader is het relevant dat hogere frequenties van *hprt* mutaties en chromosomale aberraties zijn gerapporteerd in populaties blootgesteld aan verhoogde achtergrondstraling.

Het in Hoofdstuk 7 t/m 9 beschreven onderzoek heeft betrekking op het vaststellen van een relatie tussen binnenhuisblootstelling aan radon en het voorkomen van verschillende typen van genetische schade welke beschouwd worden als vroege indicatoren voor de carcinogenese, in verschillende subpopulaties woonachtig in het grensgebied tussen Nederland en België. De onderliggende doelstelling van het onderzoek is het toetsen van het hypothetische lineaire karakter van de dosis-respons relatie op het biologische niveau.

Om een dosis-respons relatie betrouwbaar te kunnen vaststellen is het noodzakelijk om voldoende variatie in de blootstelling te verkrijgen. Een onderzoek is uitgevoerd om de radonconcentraties in het bodemgas en het binnenmilieu in dit gebied te bepalen (Hoofdstuk 6). Om een indruk te krijgen

van de radonconcentraties in woningen in de Belgische grensgemeente Visé zijn in eerste instantie in 116 woningen gedurende 24 uur radonmetingen verricht met behulp van actief kool detectie. De gemiddelde radonconcentratie bedroeg 116 Bq/m^3 (range 20-1625 Bq/m^3). De oorzaak van de relatief hoge radonconcentraties in sommige woningen in de gemeente Visé kan gezocht worden in de uranium-houdende onderlaag van de bodem. In de grensgemeente Eijsden zijn met behulp van dezelfde methode in 42 woningen de radonconcentraties bepaald (gemiddeld 46 Bq/m^3). Aanvullende radonmetingen met behulp van een alfa track detector gedurende 3 maanden leiden tot overeenkomstige resultaten. Het radongas gehalte in de bodem in de gemeente Eijsden is, in tegenstelling tot in de gemeente Visé, te laag en de spreiding te groot om als een goede voorspeller te kunnen dienen voor de radonconcentratie in de woning. Het is mogelijk gebleken om aan de hand van dit onderzoek een blootstellingsgradient van radon in het binnenmilieu te verkrijgen, welke gebruikt is voor het bepalen van de dosis-respons relatie in de Hoofdstukken 7 t/m 9.

Uit de resultaten van het haalbaarheidsonderzoek (Hoofdstuk 7) en het vervolgonderzoek (Hoofdstuk 8 t/m 9) blijkt dat er geen relatie is tussen blootstelling aan radon in het binnenmilieu en de frequentie van SCE's, micronuclei en chromosomale aberraties in perifere lymfocyten. Daarentegen blijkt de mutatie frequentie (logaritmisch getransformeerd) van het *hprt* gen in perifere lymfocyten van de blootgestelde populaties significant negatief geassocieerd te zijn met de radonconcentratie in het binnenmilieu. Aanvullend blijkt het rookgedrag en leeftijd positief geassocieerd met respectievelijk de SCE-frequentie en *hprt* mutatie frequentie.

Uit deze resultaten blijkt dat er geen lineaire relatie wordt gevonden tussen genetische schade in perifere lymfocyten en binnenhuisblootstelling aan radon. Uit dit onderzoek wordt dus geen verdere onderbouwing gevonden voor de aanwijzing verkregen via epidemiologisch onderzoek, dat blootstelling aan radon een extrapulmonair kankerrisico zou impliceren. Voorts wordt er geen evidentie verkregen voor de juistheid van lineaire extrapolatie naar het lage blootstellingsgebied in geval van carcinogene factoren, waardoor onzekerheid blijft bestaan over de risico's van radon in het lage blootstellingsgebied. Het reduceren van deze onzekerheid vormt een uitdaging voor toekomstig onderzoek.

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